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Biological Activity of the New Herbicide LGC-40863 {benzophenone *O*-[2,6-bis[(4,6-dimethoxy-2-pyrimidinyl)oxy]benzoyl]oxime}

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Abstract: Herbicidal characteristics of the experimental compound LGC-40863 (ISO proposed common name: pyribenzoxim) were investigated in greenhouse and field. In the greenhouse, LGC-40863 had strong post-emergent activity on various grass and broadleaf weeds including *Echinochloa crus-galli* L. Beauv., *Alopecurus myosuroides* Huds. and *Polygonum hydropiper* L., while it was safe in rice (*Oryza sativa* L.), wheat (*Triticum aestivum* L.) and zoysiagrass (*Zoysia japonica* Steud; (a turf species). Among important rice weeds, *E. crus-galli* was controlled over a wide window from the one-leaf to the six-leaf stages. In the field, LGC-40863 provided excellent control of *E. crus-galli* (>95%) at 30 to 40 g ha^{-1} when applied alone, or at 15 to 30 g ha^{-1} when applied in combination with pendimethalin, while it did not cause injury to rice at up to 60 g ha^{-1}. These results suggest that LGC-40863 has potential as a new selective post-emergent herbicide in rice.

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Key words: LGC-40863, pyribenzoxim, post-emergence, rice herbicide, bioactivity

1 INTRODUCTION

Since the first report of the herbicidal activity of 2-phenoxypyrimidine compounds,[1] great efforts have been made to discover useful herbicides with this chemistry. Recently, KIH-2031,[2] KIH-6127[3] and KIH-2023[4] were introduced as new acetolactate synthase (ALS)-inhibiting herbicides. This class of herbicide is classified as pyrimidyloxybenzoate or pyrimidyloxysalicyclic acid, and their structure–activity relationship has been summarized.[5] We were interested in introducing different substituents into the carboxyl group of 2-(pyrimidin-2-yl)oxybenzoic acid. We have discovered several novel oxime ester derivatives showing strong herbicidal activity and good crop selectivity.[6] The herbicidal characteristics of the example LGC-40863 (Fig. 1) are reported in this paper.

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2 MATERIALS AND METHODS

2.1 Synthesis

The carboxyl group of 2,6-bis(acetyloxy)benzoic acid (**2**) obtained by acylation of 2,6-dihydroxybenzoic acid (**1**) was activated with thionyl chloride, and subsequently esterified with benzophenone oxime (**3**) at low temperature. The resulting oxime ester (**4**) was treated with two equivalents of 4,6-dimethoxy-2-methylsulfonylpyrimidine (**5**) in the presence of potassium carbonate in dimethylformamide to yield LGC-40863 (**6**).

2.1.1 *Benzophenone* O-[*2,6-bis*(*acetyloxy*)*benzoyl*] *oxime* (*4*)

A mixture of 2,6-dihydroxybenzoic acid (1·5 g, 10 mmol) and acetic anhydride (10 ml, 0·1 mol) was heated to 80°C and stirred for 3 h. The mixture was poured into ice-water and was allowed to stand for 6 h.

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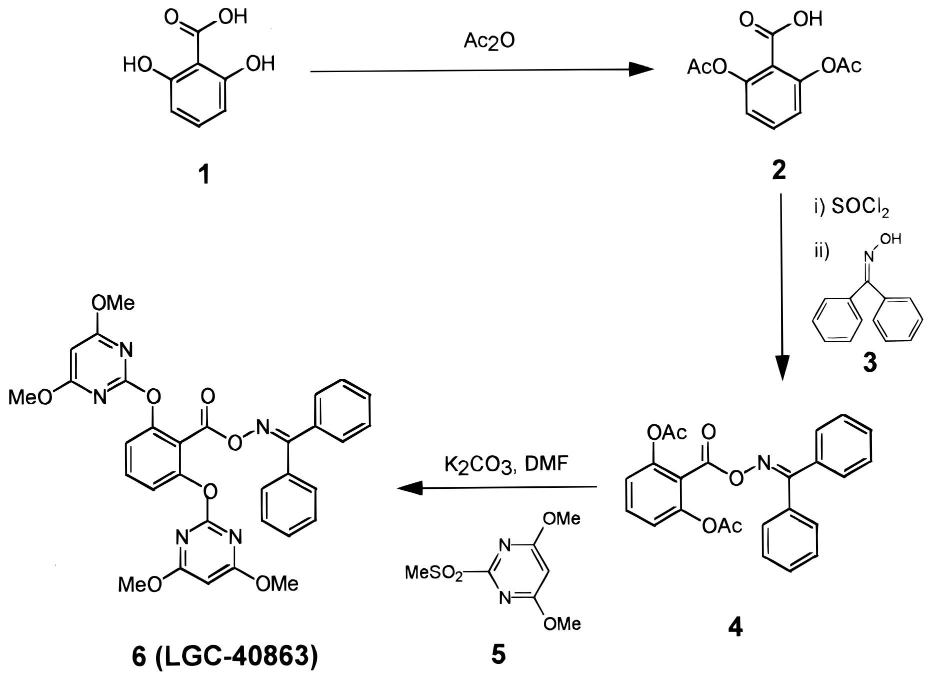

Fig. 1. Structure and synthesis scheme for LGC-40863.

The resulting white solid was filtered and dried in air to yield, 2,6-bis(acetyloxy)benzoic acid (**2**) as a white solid; 2·1 g of crude product.

Without further purification, compound **2** was dissolved in dichloromethane (5 ml). To the mixture was added dropwise a solution of thionyl chloride (1·5 ml, 20 mmol) in dichloromethane (5 ml) at 0°C. After 2 h at room temperature excess thionyl chloride and the solvent were removed. The acyl chloride was distilled from the residue. The distillate was dissolved in dichloromethane (5 ml), and to this mixture was added dropwise, a solution of benzophenone oxime (2·0 g, 10 mmol) in dichloromethane at −20°C. After 4 h at this temperature, the mixture was poured into water and extracted with ether. The combined organic layer was washed with aqueous sodium hydrogen carbonate solution and dried over magnesium sulfate. After evaporation, the residue was purified by silica gel column chromatography to yield the product (**4**); 2·7 g (65%).

[^{1}H]NMR (deuterochloroform, 300 MHz):
δ 2·12 (s, 6H), 7·00–7·58 (m, 13H)
FAB MS: 418 (M + H)

2.1.2 *Benzophenone* O-[*2,6-bis*[*(4,6-dimethoxypyrimidinyl)oxy*]*benzoyl*] *oxime* (**6**)

To a mixture of **4** (2·0 g, 4·8 mmol), potassium carbonate (1·0 g, 7·2 mmol) and dimethylformamide (5 ml) was added, portionwise, 4,6-dimethoxy-2-methylsulfonylpyrimidine (**5**) (2·1 g, 9·6 mmol) and heated to 80°C for 15 h. The resulting mixture was diluted with water (10 ml) and extracted with ether. The organic layer was washed with aqueous sodium bicarbonate solution and dried over magnesium sulfate. After evaporation the residue was purified by silica gel column chromatography to yield LGC-40863 (**6**); 1·5 g (65%).

[^{1}H]NMR (deuterochloroform, 300 MHz):
δ 3·72 (s, 12H), 5·72 (s, 2H),
7·12 (d, J = 8·4 Hz, 2H), 7·30–7·48 (m, 13H).
IR (cm^{-1}): 1760, 1610, 1580, 1475, 1350, 1250, 1190.
FAB MS: 610 (M + H).
m.p. 128–130°C.

2.2 Biological activity

2.2.1 *Plant preparation and herbicide treatment*

Seeds of various plants were sown in plastic pots (surface area: 150 to 300 cm^2) filled with sterilized silty loam soil with a composition of 43% sand, 43% silt and 14% clay, an organic matter content of 1·9% and pH 5·6. Depending on experimental objectives, each pot contained different numbers of species. The plants were grown in a greenhouse maintained at 28–33°C during the day and 20–26°C at night. After the plants reached a desirable growth stage, herbicide solutions were sprayed with a CO_2-pressurized belt-driven sprayer equipped with an 8002 flat-fan nozzle (Spraying Systems Ltd) adjusted to deliver 1000 litre ha^{-1} at 300 kPa. Herbicide solutions were prepared by dissolving technical LGC-40863 (96% purity) in acetone, and subsequently adding distilled water containing 2·0 g litre^{-1} 'Tween' 20. The resulting solutions contained 500 ml litre^{-1} acetone, 1 g litre^{-1} 'Tween' 20 and the required amounts of LGC-40863.

2.2.2 *Plant spectrum*

Thirty-three plant species listed in Table 1 were grown to the two- to three-leaf stage. LGC-40863 was then

TABLE 1
Herbicidal Activity of LGC-40863 by Post-Emergent Application in a Greenhouse

	Rate (g ha^{-1})						
Species	*2·5*	*5*	*10*	*15* (%)[a]	*20*	*30*	*60*
Crops							
Glycine max (L.) Merr.	0	20	30	70	80	80	90
Gossipium hirsutum L.	0	0	10	20	40	40	50
Oryza sativa L.	0	0	0	0	0	0	10
Triticum aestivum L.	0	0	0	0	0	0	10
Zea mays L.	0	0	30	50	70	90	90
Zoysia japonica Steud.	0	0	0	0	0	0	0
Grass Weeds							
Alopecurus myosuroides Huds.	0	0	20	70	80	100	100
Cynodon dactylon (L.) Pers.	30	50	30	50	50	70	70
Digitaria sanguinalis (L.) Scop.	0	0	40	60	60	90	100
Echinochloa crus-galli (L.) Beauv.	10	50	90	90	100	100	100
Echinochloa colona (L.) Link	40	60	70	100	100	100	100
Poa annua L.	0	0	0	20	40	40	80
Setaria viridis (L.) Beauv.	0	0	0	20	60	60	70
Broadleaf Weeds							
Abutilon theophrasti Medicus	0	0	10	10	40	50	60
Aeschynomene indica L.	10	30	80	80	100	100	100
Amaranthus retroflexus L.	10	30	80	80	100	100	100
Bidens frondosa L.	0	10	30	80	90	90	100
Cassia obtusifolia L.	0	30	50	50	60	70	80
Chenopodium album L.	0	0	0	20	20	40	40
Cirsium arvense (L.) Scop.	60	70	70	80	90	100	100
Convolvus arvensis L.	0	0	40	40	50	60	60
Galium aparine L.	20	40	30	60	80	100	100
Ipomoea nil (L.) Roth	0	0	0	20	20	50	50
Polygonum hydropiper L.	0	20	60	70	80	90	100
Portulaca oleracea L.	0	30	30	40	50	60	70
Rumex japonicus Houtt.	0	0	40	60	60	90	100
Sesbania exaltata (Raf.) Rydb. ex A. W. Hill	0	20	30	50	80	100	100
Sida spinosa L.	0	0	0	30	40	40	50
Solanum nigrum L.	10	40	90	90	100	100	100
Stellaria media (L.) Vill.	0	40	80	100	100	100	100
Taraxacum officinale Webber and Wiggers	0	20	30	30	50	60	60
Viola tricola L.	0	0	0	20	20	60	60
Xanthium strumarium L.	40	60	80	80	90	90	90

[a] Visual rating at four weeks after treatment, where 0 indicates no visible effect and 100 complete death of plants.

sprayed at application rates up to 60 g ha^{-1}. Plant responses were evaluated visually at two-day intervals based on a scale of 0 to 100, where 0 indicated no visible effect and 100 indicated complete death of plants. Final evaluation was made four weeks after treatment.

2.2.3 *Application windows for* Echinochloa crus-galli *control*

2.2.3.1 Growth-stage effects. Thirty seeds of *E. crus-galli* were sown in a pot (surface area: 150 cm^2) as described above. After germination, equal numbers of plants having a similar growth stage were retained, and grown to six different growth stages from the 1·5- to 6·5-leaf stage. LGC-40863 was sprayed at rates up to 60 g ha^{-1} at each stage. Fresh weights were measured four weeks after treatment.

2.2.3.2 Comparison with propanil (3′,4′-dichloro-propionanilide). Four different stages of *E. crus-galli*, the 1·5-, 3-, 4·5- and 6·5-leaf stages, were grown as described above. LGC-40863 (20 g ha^{-1}) or propanil (1500 g ha^{-1}) were sprayed at each stage. Fresh weights were measured four weeks after treatment. These experiments were conducted in a completely randomized

design, and each treatment was replicated six times. Data were subjected to analysis of variance.

2.2.4 Determination of field rates

A field experiment was conducted in 1995 at the LG Chem Research Park, Taejon, Korea. The soil was a silty to sandy loam soil with a composition of 51% sand, 39% silt and 10% clay, an organic matter content of 1·4%, and pH 5·5. The field was rotavated and levelled in dry conditions, and rice (cv. Ilpum) was seeded at 50 kg ha^{-1} to a depth of 3 to 5 cm with 30-cm row spacing on 4 May. Weed germination was based on natural emergence, and consisted of *E. crus-galli* (>80%), *P. hydropiper* (>10%) and some other broadleaf weeds. Herbicide was applied with a CO_2-pressurized backpack sprayer equipped with 8002 flat-fan nozzles adjusted to deliver 1000 litre ha^{-1} at 300 kPa (conventional spray volume in Korea). Formulated LGC-40863 (10 g $litre^{-1}$ EC) was used for this study. Treatments included LGC-40863 at up to 60 g AI ha^{-1}, and tank-mixes of LGC-40863 plus pendimethalin [*N*-(1-ethylpropyl)-2,6-dinitro-3,4-xylidine] (317 g $litre^{-1}$ EC; Sam-Kong, Korea) at the rates described in Table 2. A pre-mixed formulation of propanil plus pendimethalin (200 + 250 g $litre^{-1}$ EC; Sam-Kong, Korea) was also treated at recommended and double recommended rates as commercial standards. LGC-40863 and its tank-mixes with pendimethalin were sprayed on 24 May, when *E. crus-galli* was grown to the three- to four-leaf stage. The pre-mix of propanil plus pendimethalin was sprayed earlier, on 19 May, as recommended. Evaluation was made 30 days after treatment. Herbicidal efficacy was assessed by measuring the fresh weight of weeds in three quadrats (20 cm wide × 50 cm long) in each plot. Among weeds, *E. crus-galli* was separately measured, while others were combined. Rice phytotoxicity was evaluated visually on a scale of 0 to 100, where 0 indicated no visible effect and 100 indicated complete death of plants. The field was occasionally irrigated until 30 days after seeding, and was maintained in flooded conditions afterwards. A complete fertilizer was applied three times in the season providing total N : P : K at 160 : 70 : 80 kg ha^{-1}, respectively. Each individual plot was 3 m wide × 7 m long. Experimental design was a randomized complete block with four replications. Data were subjected to analysis of variance.

3 RESULTS

3.1 Plant spectrum and herbicidal symptoms to LGC-40863

Among crops, soybean (*G. max*) and corn (*Z. mays*) were susceptible, while rice (*O. sativa*), wheat (*T. aestivum*) and zoysiagrass (*Z. japonica*) were tolerant (Table 1). Cotton showed intermediate tolerance. Various weeds were controlled by LGC-40863 at 10 to 60 g ha^{-1}. Many important grass weeds including *A. myosuroides*, *D. sanguinalis*, *E. crus-galli* and *E. colona* were controlled >80% at 10 to 30 g ha^{-1}. Among

TABLE 2

Herbicidal Efficacy and Rice Phytotoxicity of LGC-40863 at 30 Days after Treatment in a Dry Direct-Seeded Field Test

Treatment	*Application*		*Weed fresh weight*			*Rice injury (%)*[b]
	Rate (g/ha^{-1})	*Time (DAS)*[a]	E. crus-galli ($g\ m^{-2}$)	*Others ($g\ m^{-2}$)*	*Control value (%)*	
LGC-40863	15	20	47·5	12	63·9	0
LGC-40863	20	20	27·5	6	80·0	0
LGC-40863	30	20	6·3	1	95·6	0
LGC-40863	40	20	6·0	1	96·3	0
LGC-40863	60	20	—	—		12·5
LGC-40863 + pendimethalin	15 + 1250	20	16·3	2	88·9	0
LGC-40863 + pendimethalin	20 + 1250	20	15·0	2	89·6	0
LGC-40863 + pendimethalin	30 + 1250	20	5·9	1	95·8	0
LGC-40863 + pendimethalin	40 + 1250	20	5·5	0	96·6	5
LGC-40863 + pendimethalin	60 + 2500	20	—	—		10
Propanil + pendimethalin	1250 + 1250	15	9·3	10	88·3	0
Propanil + pendimethalin	2500 + 2500	15	—	—		17·5
Hand weeding (at 20 DAS)		—	13·6	3·5	89·6	0
Untreated control		—	125	40	—	—
LSD 0·05			101	3·8	8·4	2·1

[a] DAS: days after seeding.
[b] Visual rating, where 0 indicates no visible effect and 100 complete death of plants.

broadleaf weeds, *A. indica*, *A. retroflexus*, *B. frondosa*, *C. arvense*, *G. aparine*, *P. hydropiper*, *R. japonicus*, *S. nigrum*, *S. media* and *X. strumarium* were controlled at similar rates. Least susceptible weeds tested were *C. album*, *I. nil* and *S. spinosa*. In a similar experiment, LGC-40863 showed no pre-emergence activity against these species (data not shown). These results show that LGC-40863 is a broad-spectrum herbicide having strict post-emergent activity, and indicate that this compound may have potential as a selective herbicide for rice, wheat and zoysiagrass.

Figure 2 describes the progression of herbicidal symptom development in *E. crus-galli*. In the first week after herbicide application, few herbicidal symptoms were observed in plants except for slight stunting, while during the second week, *E. crus-galli* and other susceptible weeds were killed. Therefore, LGC-40863 appeared to be a relatively slow-acting herbicide. Herbicidal symptoms in susceptible grasses included plant stunting followed by chlorosis and finally desiccation of the whole plant.

3.2 Growth stage effects on *Echinochloa crus-galli* control

Application rate responses of *E. crus-galli* were determined from the 1·5- to 6·5-leaf stage (Fig. 3). Among the growth stages tested, the 2·5- and 3·5-leaf stages were most sensitive (complete control at 10 g ha^{-1}) followed by the 1·5- and 4·5-leaf stages (complete control at 20 g ha^{-1}), and the 5·5- and 6·5-leaf stages (> 95% control at 30 g ha^{-1}). This result indicates that, although the optimum time of LGC-40863 application is between the 2·5- and 3·5-leaf stage for *E. crus-galli*, the application widow of LGC-40863 can be extended up to the six-leaf stage by increasing the application rate. Therefore, LGC-40863 could provide great flexibility to farmers' application timings. This was further demonstrated in comparison with propanil, which is widely used for *E. crus-galli* control (Fig. 4). Propanil controlled young *E. crus-galli* (1·5-leaf stage) effectively, but its efficacy decreased dramatically with increasing plant size. Therefore, the application timing of propanil is limited to early stage *E. crus-galli*. By comparison, LGC-40863 provided good to complete control of *E. crus-galli* up to the six-leaf stage. This result shows that LGC-40863 has a much wider application window than propanil.

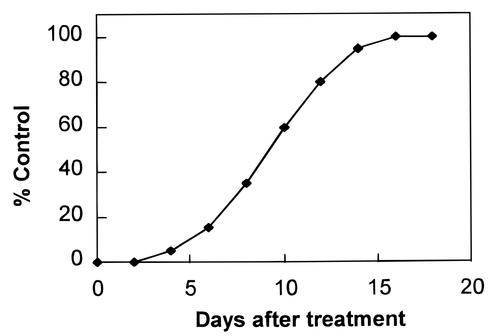

Fig. 2. Time-course changes of herbicidal activity of LGC-40863 on *Echinochloa crus-galli*.

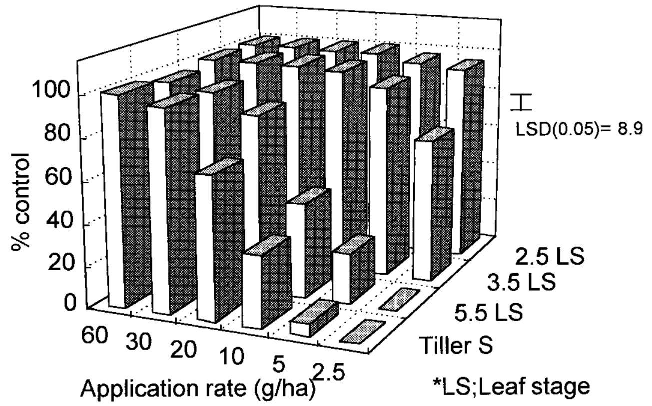

Fig. 3. Control of *Echinochloa crus-galli* by LGC-40863 at various growth stages.

3.3 Determination of field rates

The herbicidal efficacy and phytotoxicity of LGC-40863 were evaluated in a dry-seeded condition. LGC-40863 applied alone gave insufficient weed control at rates lower than 20 g ha^{-1} (Table 2). However, the herbicide provided excellent weed control (>95%) at 30 to 40 g ha^{-1}. Because LGC-40863 has no pre-emergence activity, it would be desirable to adopt a pre-emergence herbicide partner for persistent weed suppression. When LGC-40863 was applied in combination with pendimethalin, a pre-emergence herbicide, herbicidal efficacy increased considerably, providing good control (89%) even at 15 to 20 g ha^{-1}, where it was insufficient when treated alone. At higher rates (30 to 40 g ha^{-1}), however, there was no significant additional effect from pendimethalin because LGC-40863 alone provided excellent weed control. There was little or no rice injury at up to 60 g ha^{-1} LGC-40863, either treated alone, or in mixture with pendimethalin. These results again demonstrate that LGC-40863 can be used as a selective herbicide for rice, particularly in a dry-seeded condition.

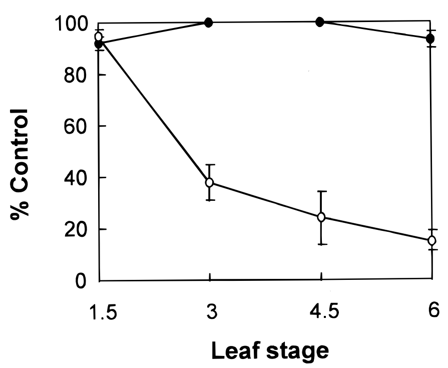

Fig. 4. Growth stage effects on *Echinochloa crus-galli* control by (●) LGC-40863 (20 g ha^{-1}) and (○) propanil (1500 g ha^{-1}).

The use rate of LGC-40863 appeared to be about 30 g ha^{-1} when applied alone, while it could be reduced when pendimethalin was added.

4 DISCUSSION

Pyrimidyloxybenzoates are a relatively new herbicide class, and their mode of action is known to be inhibition of ALS, similar to that of sulfonylurea and imidazolinone herbicide.[5] In this chemistry, pyrithiobac is used as a cotton herbicide,[7] while KIH-2023 and KIH-6127 have been introduced as rice herbicides.[3,4] Because LGC-40863 is structurally related to this class of herbicide, it is speculated that its mode of action is similar to that of other ALS-inhibitors. LGC-40863 controlled various grass and broadleaf weeds at low rates (below 60 g ha^{-1}), at the same time showing a high level of safety in rice, wheat and zoysiagrass. Relatively few herbicides are available for selective control of *E. crus-galli* in rice, particularly among ALS-inhibiting herbicides, but LGC-40863 controlled *E. crus-galli*, the most troublesome weed, as well as various important broadleaf weeds including *P. hydropiper*, *B. frondosa* and *A. indica.* Because LGC-40863 appears to be physiologically selective between rice and *E. crus-galli*, this molecule could be regarded as an advance in ALS-inhibitor chemistry.

Because LGC-40863 is a post-emergent herbicide, flexibility in application time is an important factor, giving a possible application window from the one- to six-leaf stage of *E. crus-galli.* It usually takes at least one month for *E. crus-galli* to grow from the one- to the six-leaf stage in field conditions. Therefore, LGC-40863 could be applied with great time flexibility. This aspect is notably advantageous when compared to the narrow and limiting application window of propanil for *E. crus-galli* control. However, this flexibility remains to be examined under field conditions.

In field conditions, LGC-40863 was effective at 30 g ha^{-1} when applied alone. This rate could be reduced further when used in combination with a partner herbicide. The rate of LGC-40863 was, therefore, similar both in the greenhouse and in the field, suggesting that its herbicidal efficacy is consistent across widely differing conditions.

Despite the high post-emergence activity, LGC-40863 had almost no pre-emergence or soil activity. This may be due in part to tight binding of the molecule to the soil matrix, and/or the relatively short half-life in soil; $t_{1/2}$ = six days (Koo *et al.*, unpublished data). Consequently, LGC-40863 caused no carry-over injury to following crops in either greenhouse or field studies (data not shown).

In summary, LGC-40863 was shown to be a broad-spectrum post-emergence herbicide with a high level of selectivity in rice. It had a low use rate (around 30 g ha^{-1}), and the application time was greatly flexible. In addition, the herbicide was safe to rotational crops. Therefore, LGC-40863 could be used as a new tool for weed management in rice culture, particularly in direct-seeded conditions. LGC-40863 also had safety to wheat and zoysiagrass (a turf species). The potential for these species remains to be evaluated.

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